

Talking about the genetics of talking: the discovery of the first "speech and language" gene

Created: November 1, 2003



The ability to articulate speech includes performing complex orofacial movements.

Chimpanzees and other great apes lack this ability.

Language has played a fundamental role in human cultural evolution. The ability of humans to speak involves fine motor control of the larynx and mouth; this control is absent in other primates.

Individuals with specific language impairment (SLI) have a developmental disorder of speech and language that is not attributable to deafness, autism, or any other general causes. Examples of symptoms include problems in articulation, identification of basic speech sounds, and understanding sentences and grammar. Although SLI does run in families, the inheritance patterns are usually complex, and until recently, little could be said about its genetic basis.

This changed with the study of a British family known as "KE". Several generations of this family were affected by SLI which was inherited in an autosomal dominant fashion. In 1998, this disorder was linked to a small segment of chromosome 7, labeled SPCH1. Then came the discovery of CS, an unrelated person who had a SLI, similar to that of the KE family and had a chromosomal translocation

involving the SPCH1 interval. The discovery of CS helped to narrow the language disorder to a specific gene, FOXP2 (forkhead box P2).

FOXP2 belongs to a family of genes that encodes transcription factors (proteins that regulate the expression of genes). FOXP2 contains a forkhead domain that binds to DNA. The forkhead domain is disrupted in CS by translocation breakpoint, and in the KE family by a point mutation. Lai *et al.* propose that such a disruption in this region alters the DNA-binding and/or transactivation properties of FOXP2. There is some evidence that the FOXP2 gene is a key part of human evolution. For example, the protein product is almost identical in mice, monkeys, and apes, which are separated by 130 million years of evolution. But humans differ from these species in two or three amino acids, through mutations estimated to have occurred within the last 200,000 years.

What is the role of FOXP2? We know that forkhead domain transcription factors have many important roles in the regulation of the development of embryos. Indeed, FOXP2 is expressed in fetal tissue, including the developing brain.

Enard *et al.* suggest that FOXP2 is needed in the development of the normal brain circuitry that underlies language and speech. They propose that at a critical point in fetal brain development, affected individuals have only half the normal amount of functioning transcription factor, which is not enough for normal early brain development.

FOXP2 is the first gene to be directly linked to speech and language disorders. Whatever the exact function of the gene turns out to be, it is unlikely that only one gene is responsible for speech. However,

this discovery of a genetic component fuels the search for genetic causes of other cognitive and learning disorders.

Important Links

Live PubMed searches

- (1) FOXP2 mutations
- (2) Specific language impairment
- (3) REVIEWS

Further NCBI resources

- OMIM
- LocusLink
- Genome view

Box: A Gene involved in Speech?

Taking a closer look at the forkhead domain.

For this tutorial, you will need to have flash [<http://www.macromedia.com/go/getflashplayer>] installed on your computer.

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